REMARKS

I. Introduction

Claims 1-9, 13-15, 20-23 were under examination. In this amendment, claims 8-9, 13-14, 20 and 23 are cancelled, claims 1-4, 7, 15, and 21-22 are amended, and claims 33-34 are added. Upon entry of the amendment claims 1-7, 15, 21-22 and 33-34 will be pending. The amendment or cancellation of claims by this amendment is without prejudice to future prosecution of similar claims in this or a related application, and does not indicate acquiescence with any position taken by the Office.

Applicants thank Examiner Saunders for conducting an examination of all claims of Group 1 even though the examiner was of the opinion that the elected species, fibulin-6 is recited "nowhere in the disclosure." (Fibulin-6 is recited on page 33; fibulin mRNA expression in human eye tissues is described.) Applicants have now amended the claims to focus the prosecution on the autoimmune response to specific drusen and RPE proteins. Should the Examiner have any questions please contact the undersigned.

Applicants have discovered that autoantibodies against several specific drusen and RPE proteins are found in serum of patients with macular degenerative disorders, including beta-crystallins, calrecticulin, 14-3-3 protein epsilon, or serotransferrin and fibulin-3 (see, e.g., Examples 3, 4 and 6; pages 27-31, and 35). To expedite the present prosecution, the claims have been amended to focus on diagnostic methods in which autoantibodies to *fibulin-3, beta-crystallin A2, beta-crystallin A3, beta-crystallin A4, beta-crystallin S, calrecticulin, 14-3-3 protein epsilon,* or *serotransferrin*, or immune complexes containing one of these proteins or an antigenic fragment are detected. Support for the amendments is replete in the specification. See, e.g., the specification at page 12, first full paragraph.

II. Claim Rejections under 35 U.S.C. § 112, Second Paragraph

Claim 9 was rejected as lacking antecedent basis. Claim 9 has been amended to overcome this rejection.

III. Claim Rejections under 35 U.S.C. § 112

A. Written Description

Claims 1-9, 14-15, 20, 21 and 23 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The Office believes the Applicants have not adequately described the genus of "macular degeneration associated molecules." Applicants respectfully disagree. However, to expedite prosecution, the pending claims have been amended to remove this phrase and are directed to detecting autoantibodies or immune complexes related to the specific proteins *fibulin-3, beta-crystallin A2, beta-crystallin A3, beta-crystallin A4, beta-crystallin S, calrecticulin, 14-3-3 protein epsilon,* or *serotransferrin.*

The rejection of claims 2, 14 and 23 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement is moot in view of the amendment of claim 2 and cancellation of claims 14 and 23.

Applicants respectfully request withdrawal of the rejection.

B. Enablement

Claims 1-9, 13-15, 20, 21 and 23 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly not enabled by the specification. The pending claims, as amended, are now focused on an autoimmune response to particular proteins. The specification clearly discloses that autoantibodies to proteins such as *fibulin-3, beta-crystallin A2, beta-crystallin A3, beta-crystallin A4, beta-crystallin S, calrecticulin, 14-3-3 protein epsilon,* and *serotransferrin* are found in serum from patients with macular degeneration related disorders, and described diagnostic assays for autoantibodies and immune complexes (see specification at, , e.g., pages 14-17 and Examples 3, 4 and 6). The claims, as amended, are now directed to detection of autoantibodies and immune complexes related to these proteins.

Applicants respectfully request withdrawal of the rejection.

IV. Claim Rejections under 35 U.S.C. § 102 (b) and/or 103(a)

Claims 1-3, 5-7, 13, 15 and 20-22 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by International Publication No. WO 95/17673 ("Hageman"). Claims 1, 3, 8 and 9 were rejected under 35 U.S.C. § 103(a) as allegedly obvious over Hageman in view of U.S. Patent No. 3,654,090 ("Schuurs"). Hageman is asserted to describe diagnosis of early AMD by detecting the presence of *vitronectin* autoantibodies. The claims, as amended, no longer recite vitronectin. Accordingly, Applicants believe this rejection is overcome.

Claims 1-3, 5-7, 15, 20 and 21 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as allegedly obvious over Penfold et al. Penfold is relied on for description of antibodies to *glial fibrillary acid protein*. Penfold did not describe or suggest a relationship between an immune response to *fibulin-3, beta-crystallin A2, beta-crystallin A3, beta-crystallin A4, beta-crystallin S, calrecticulin, 14-3-3 protein epsilon,* or *serotransferrin* and macular degeneration. Accordingly, Applicants believe this rejection is overcome.

Claims 1, 3, 5-7, 15, 20 and 21 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as allegedly obvious over, Gurne et al. ("Gurne"). Claims 1-3, 5-7, 15, 20 and 21 were also rejected under 35 U.S.C. § 102(b) as allegedly anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as allegedly obvious over the article by Chen et al. ("Chen").

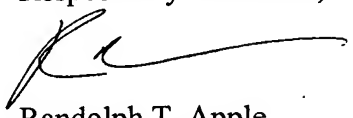
Both Gurne and Chen are relied on for descriptions of autoantibodies against unidentified retinal proteins from subjects with age-related macular degeneration. However, nothing in either Gurne or Chen described or suggested the instantly claimed method of diagnosing or identifying a predisposition to the development of, a macular degeneration related disorder in a subject by detecting in the presence or abnormal levels of an autoantibody against, or an immune complex

containing, *fibulin-3, beta-crystallin A2, beta-crystallin A3, beta-crystallin A4, beta-crystallin S, calrecticulin, 14-3-3 protein epsilon,* or *serotransferrin*. Chen described immunoreaction of serum antibodies with at least five apparently different proteins from retinal homogenates, none of them identified as *fibulin-3, beta-crystallin A2, beta-crystallin A3, beta-crystallin A4, beta-crystallin S, calrecticulin, 14-3-3 protein epsilon,* or *serotransferrin*. Gurne described immunoreaction of serum antibodies with an unidentified protein suspected of being a cytoskeletal protein or degradation product of a cytoskeletal protein (see page 606, sentence spanning columns 1 and 2) identified as having a molecular weight of about 58-62 kD and localized within the outer segments of visual cells. Gurne did not suggest that autoantibodies to *fibulin-3, beta-crystallin A2, beta-crystallin A3, beta-crystallin A4, beta-crystallin S, calrecticulin, 14-3-3 protein epsilon,* or *serotransferrin* are present in patients with or susceptible to macular degeneration disorders. Neither Chen nor Gurne described or suggested a diagnostic method as now claimed, nor would a scientist of ordinary skill in the art have found a suggestion for such a diagnostic method in these references. For this reason, Applicants respectfully request this rejection be withdrawn.

V. Conclusion

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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